PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY
(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 32993-74744	FOR FURTHER ACTION	See Form PCT/IPEA/416
International application No. PCT/US04/08477	International filing date *(day/month/year)* 19 March 2004 (19.03.2004)	Priority date *(day/month/year)* 20 March 2003 (20.03.2003)
International Patent Classification (IPC) or national classification and IPC IPC(7): C12Q 1/54 and US Cl.: 435/14		
Applicant ADVANCED RESEARCH AND TECHNOLOGY INSTITUTE, INC.		

1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 6 sheets, including this cover sheet.
3. This report is also accompanied by ANNEXES, comprising:
   a. ☐ *(sent to the applicant and to the International Bureau)* a total of ___ sheets, as follows:
      ☐ sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).
      ☐ sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.
   b. ☐ *(sent to the International Bureau only)* a total of (indicate type and number of electronic carrier(s)) _____, containing a sequence listing and/or tables related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).
4. This report contains indications relating to the following items:
   - ☒ Box No. I Basis of the report
   - ☐ Box No. II Priority
   - ☐ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - ☒ Box No. IV Lack of unity of invention
   - ☒ Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - ☐ Box No. VI Certain documents cited
   - ☐ Box No. VII Certain defects in the international application
   - ☐ Box No. VIII Certain observations on the international application

Date of submission of the demand	Date of completion of this report
08 April 2005 (08.04.2005)	19 July 2005 (19.07.2005)
Name and mailing address of the IPEA/ US Mail Stop PCT, Attn: IPEA/US Commissioner for Patents P.O. Box 1450 Alexandria, Virginia 22313-1450 Facsimile No. (703) 305-3230	Authorized officer Jennifer Ione Harle Telephone No. (571) 272-1600

Form PCT/IPEA/409 (cover sheet)(January 2004)

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/US04/08477

Box No. I Basis of the report

1. With regard to the **language**, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ This report is based on translations from the original language into the following language _____, which is the language of a translation furnished for the purposes of:

☐ international search (under Rules 12.3 and 23.1(b))

☐ publication of the international application (under Rule 12.4)

☐ international preliminary examination (under Rules 55.2 and/or 55.3)

2. With regard to the elements of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report)*:

☒ the international application as originally filed/furnished

☒ the description:
pages 1-16 as originally filed/furnished
pages* NONE received by this Authority on _____
pages* NONE received by this Authority on _____

☒ the claims:
pages 17-19 as originally filed/furnished
pages* NONE as amended (together with any statement) under Article 19
pages* NONE received by this Authority on _____
pages* NONE received by this Authority on _____

☒ the drawings:
pages 1-2 as originally filed/furnished
pages* NONE received by this Authority on _____
pages* NONE received by this Authority on _____

☐ a sequence listing and/or any related table(s) - see Supplemental Box Relating to Sequence Listing.

3. ☐ The amendments have resulted in the cancellation of:

☐ the description, pages _____
☐ the claims, Nos. _____
☐ the drawings, sheets/figs _____
☐ the sequence listing (*specify*): _____
☐ any table(s) related to the sequence listing (*specify*): _____

4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).

☐ the description, pages _____
☐ the claims, Nos. _____
☐ the drawings, sheets/figs _____
☐ the sequence listing (*specify*): _____
☐ any table(s) related to the sequence listing (*specify*): _____

** If item 4 applies, some or all of those sheets may be marked "superseded."*

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
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Box No. IV Lack of unity of invention

1. ☒ In response to the invitation to restrict or pay additional fees the applicant has:

   ☐ restricted the claims.

   ☐ paid additional fees.

   ☐ paid additional fees under protest.

   ☒ neither restricted nor paid additional fees.

2. ☐ This Authority found that the requirement of unity of invention is not complied with and chose, according to Rule 68.1, not to invite the applicant to restrict or pay additional fees.

3. This Authority considers that the requirement of unity of invention in accordance with Rules 13.1, 13.2 and 13.3 is:

   ☐ complied with.

   ☒ not complied with for the following reasons:

See the lack of unity section of the International Search Report(Form PCT/ISA/210)

4. Consequently, this report has been established in respect of the following parts of the international application:

   ☐ all parts

   ☒ the parts relating to claims Nos. 1-8

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/US04/08477

Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims 5, 7-8	YES
	Claims 1-4, 6	NO
Inventive Step (IS)	Claims NONE	YES
	Claims 1-8	NO
Industrial Applicability (IA)	Claims 1-8	YES
	Claims NONE	NO

2. Citations and Explanations (Rule 70.7)
Please See Continuation Sheet

Supplemental Box

In case the space in any of the preceding boxes is not sufficient.

Continuation of:

V. 2. Citations and Explanations:
Claims 1-4 and 6 lack novelty under PCT Article 33(2) as being anticipated by Charkoudian, et al. (US 5,543,054).

Charkoudian discloses a composition for use in analyzing oligosaccarides, i.e. N-acetylglucosamine oligomers prepared as an aqueous solution (comprising a buffer), to which the oligo labeling dye ANTS (a derivatizing agent capable of forming one or more fluorescing carbohydrate derivatives from the one or mor ecarbohydres was added) and the reducing agent of soium cyanoborohydrde in dimethylsulfoxide (DMSO - a solvent) were added and incubated resulting in fluorescent band conjugateted tera-, penta-, hexa- and heptamers (carbohydrate derivatives), e and each sample was dissolved in Milli-Q water and 2X loading buffer. See col. 19, lines 1-20.

Claims 3-8 lack an inventive step under PCT Article 33(3) as being obvious over Charkoudian, et al. (5,543,054 A) in view of Wang, et al. Analysis of Chitin Oligosaccarides by Capillary Electrophoresis with Laser-Induced Fluorescence, Journal of Chromatography A, 2002, Vol. 979, pp. 431-438 and further in view of DMSO, Registry Information, November 15, 1984.

Charkoudian discloses as set forth above. However, Charkoudian does not disclose that the derivatizing agent can be 9-aminopyrene-1,4,6-trisulfonic acid, which is capable of forming one or more fluorescing carbohydrate derivates that are detectable by laser-induced fluorescence or that the buffer comprises a buffering agent selected from the group consisting of citric acid and salts there of. Wang discloses a method and the compounds utilized in the method using capillary electrophoresis (CE) with laser-induced fluorescence (LIF) detection for analyzing chitin oligosaccharides which were derivatized with 9-aminopyrene-1,4,6,trisulfonate, i.e. forms the acid in water. Abstract. Wang additionally discloses that chitin-oligosaccharides and related derivatives, which are amino polysaccharides have distinctive properties including a variety of biological activities and the fact that they are biodegradable into monomers, dimmers, trimers, tetramers, pentamers, and hexamers through ATPS derivatization. Pp. 431 and 436. Wang further discloses that carbohydrates generally do not contain chromophoric or fluorphoric groups and, as a result the determination of these compounds can be challenging, however, CE has attracted considerable amount of attention because of its high sensitivity, rapid analysis time, and high resolution and when used in conjunction with indirect detection, i.e. LIF due to its inherently high sensitivity/good specificity/and a large linear dynamic range , is a universal method and can be used for carbohydrate analysis. Wang discloses that the introduction of 9-aminopyrene-1,4,6,trisulonate for the CE-LIF of mono-and oligosaccharides observed a substantially higher molar absorptivity and quantum efficiency than most of the commonly used fluorphore carbohydrate derivatives and the presence of negatively charge functional groups appears to enhance the separation of mon0- and oligosaccharides. Pp. 431-432. Moreover, Wang discloses that the oligosaccharides were dissolved in water and then was mixed with ATPS and glacial acetic acid (solvent) and aqueous sodium cyanoborohydride, which was incubated and then diluted with a borate buffer and stored prior to CE separation, noting that the ionic strength of each buffer was adjusted so as to be approximately equal, in the acidic citric acid-phosphate buffer solutions, the electrophoretic mobility of th APTS-chitin oligosaccharides toward the outlet (anode is provide by negatively charged sulfonate groups under the negative applied voltage, i.e

Supplemental Box

the migration sequence of analytes to the anode is based upon their apparent electrophoretic mobility. Registry information for DMSO disloses that its properties as a solvent are similar to that of glacial acetic acid, the bcfs are very similar, they have high boiling points under the same conditions, they both accept at least one H, and their molar solubility is >=1 at the same pH ranges. Additionally, they are both utilized in the same reactions and thus their interchangeabilty would be obvious to one of ordinary skill in the art at the time of the invention. It would have been obvious to utilize 9-aminopyrene-1,4,6-trisulfonate (it would be in acid form in the reaction as it is in water) as the derivating agent capable of forming one or more fluorescing carbohydrate derivatives that are detectable by laser-induced fluorescence and the citric acid-phosphate buffer as taught by Wang in the composition of Charkoudian for the explicit reasons set forth in Wang.

Claims 1-8 meet the criteria set out in PCT Article 33(4), and thus there is industrial applicability because the subject matter claimed can be made or used in industry.